

That what is claimed is

1. A method for rank ordering characteristic signatures of cell properties, said method comprising the steps of:

forming a plurality of characteristic signatures for a plurality of cell properties having been measured from a plurality of samples taken from a heterogeneous tissue region, wherein the heterogeneous tissue region includes a first portion having at least first and second types of tissue, bordered by a second portion, said second portion considered to be devoid of the second type of tissue, wherein the plurality of samples have been taken from successive locations along a determined profile of locations through the heterogeneous tissue region, with at least one sample being taken from the second portion, and wherein each of said characteristic signatures characterizing one of the plurality of properties, respectively;

providing a trend profile of cell activity for the second type of tissue along the determined profile of locations through the heterogeneous tissue region;

performing statistical analysis on each of the plurality of characteristic signatures with regard to the provided trend profile; and

rank ordering the plurality of characteristic signatures based on proximity to the trend profile as determined by the statistical analysis.

2. The method of claim 1, further comprising the step of:

measuring the plurality of cell properties for each of the plurality of samples.

3. The method of claim 1, further comprising the steps of:

providing the heterogeneous tissue region: and

taking the plurality of samples from the heterogeneous tissue region.

4. The method of claim 3, further comprising the step of:

measuring the plurality of cell properties for each of the plurality of samples.

5. The method of claim 1, wherein the step of forming a plurality of characteristic signatures includes normalizing each of the plurality of characteristic signatures with respect to a baseline reference signature, said baseline reference signature corresponding to a measured property of a sample taken from the second portion.

6. The method of claim 1, wherein the step of performing statistical analysis includes:

comparing each of the plurality of characteristic signatures with the provided trend profile by curve-fitting to a statistical regression function, wherein said curve-fitting determines the degree of proximity of each of the plurality of characteristic signatures to the provided trend profile.

7. The method of claim 1, wherein the step of performing statistical analysis includes:

calculating a p-value with regard to each of the plurality of characteristic signatures, to test the null hypothesis between each of the plurality of characteristic signatures and the provided trend profile.

8. The method of claim 1, wherein the step of performing statistical analysis is done in one-, two- or three-dimensional space.

9. The method of claim 1, wherein the first type of tissue is healthy tissue.

10. The method of claim 1, wherein the second type of tissue is diseased tissue.

11. The method of claim 1, wherein one of the plurality of properties is an expression level of a gene.

12. The method of claim 2, wherein the step of measuring a plurality of

properties includes:

processing each of the plurality of samples using a microarray technique.

13. The method of claim 2, wherein the step of measuring a plurality of properties includes:

processing each of the plurality of samples on a single two-color microarray, two single-color microarrays or both.

14. A method comprising forwarding a result obtained from the method of claim 1 to a remote location.

15. A method comprising transmitting data representing a result obtained from the method of claim 1 to a remote location.

16. A method comprising receiving a result obtained from a method of claim 1 from a remote location.

17. A computer readable medium carrying one or more sequences of instructions for rank ordering characteristic signatures of cell properties measured from a plurality of samples taken from a heterogeneous region, wherein a first portion of the heterogeneous tissue region has at least first and second types of tissue and is bordered by a second portion of the heterogeneous tissue region, wherein the second portion is considered to be devoid of the second type of tissue, and wherein the plurality of samples have been taken from successive locations along a determined profile of locations through the heterogeneous tissue region, with at least one sample being taken from the second portion, wherein execution of one or more sequences of instructions by one or more processors causes the one or more processors to perform the steps of:

forming a plurality of characteristic signatures using the measured plurality of properties, each of said characteristic signatures characterizing one of the plurality of

properties, respectively;

providing a trend profile of cell activity for the second type of tissue along the determined profile of locations through the heterogeneous tissue region;

performing statistical analysis on each of the plurality of characteristic signatures with regard to the provided trend profile; and

rank ordering the plurality of characteristic signatures based on proximity to the trend profile as determined by the statistical analysis.

18. A system for rank ordering characteristic signatures of cell properties generated from tissue samples taken from a heterogeneous tissue region, wherein a first portion of the heterogeneous tissue region has at least first and second types of tissue and is bordered by a second portion of the heterogeneous tissue region, wherein the second portion is considered to be devoid of the second type of tissue, the system comprising:

means for providing a trend profile of cell activity for the second type of tissue along a determined profile of locations through the heterogeneous tissue region from which tissues samples are taken as the sources of the characteristic signatures;

means for performing statistical analysis on each of the plurality of characteristic signatures with regard to the provided trend profile; and

means for rank ordering the plurality of characteristic signatures based on proximity to the trend profile as determined by the statistical analysis.

19. The system of claim 18, further comprising

means for forming the plurality of characteristic signatures based on measurements of a plurality of properties characteristic of the tissues, each of said characteristic signatures related to a corresponding one of the plurality of properties.

20. The system of claim 18, further comprising:

means for measuring the plurality of properties for each of the plurality of samples.

21. A method for validating or calibrating a plotted curve of sorted p-values against the ranks of the p-values based on the order of the sorted p-values, wherein the p-values are calculated with regard to characteristic signature profiles each generated from a plurality of property values from a plurality of samples, and wherein each said p-value, as statistically calculated, represents the probability that the corresponding characteristic signature profile does not match a predefined signature profile, said method comprising the steps of :

- selecting a plurality of characteristics from a set of characteristic properties from the samples;

- preparing a sample as a mixture having two types of tissue mixed at a controlled mixture ratio;

- measuring the selected characteristics in the prepared mixture;

- repeating said preparing and measuring steps, while varying the controlled mixture ratio with each repetition of said preparing and measuring steps;

- generating a trend profile model based on the controlled variations in the mixture ratios;

- calculating a plurality of model p-values, each model p-value generated based on a comparison between a characteristic response signature, generated from characteristic values of one of the selected characteristics across all samples, with the trend profile model;

- sorting the calculated model p-values; and

- plotting the sorted model p-values against the ranks of the sorted p-values, based on the order of the sorted p-values.

22. The method of claim 21, wherein said model p-values are plotted in a logarithmic scale

23. The method of claim 21, wherein the step of preparing a mixture comprises picking a sample from a heterogeneous tissue sample having the two types

of tissue.

24. The method of claim 21, wherein the characteristics are gene expression levels, said gene expression levels being processed to form said characteristic signatures comprising gene expression response signatures.

25. The method of claim 24, wherein the measured expression levels are further processed to normalize the measured expression levels with respect to a corresponding baseline reference signature, said corresponding baseline reference signature being a measured gene expression level of one of the two types of tissue.

26. A computer readable medium carrying one or more sequences of instructions for validating or calibrating a plotted curve of sorted p-values against the ranks of the p-values based on the order of the sorted p-values, wherein the p-values are calculated with regard to characteristic signature profiles each generated from a plurality of property values from a plurality of samples, and wherein each said p-value, as statistically calculated, represents the probability that the corresponding characteristic signature profile does not match a predefined signature profile, wherein execution of one or more sequences of instructions by one or more processors causes the one or more processors to perform the steps of:

- selecting a plurality of characteristics from a set of characteristic properties from the samples;

- preparing a sample as a mixture having two types of tissue mixed at a controlled mixture ratio;

- measuring the selected characteristics in the prepared mixture;

- repeating said preparing and measuring steps, while varying the controlled mixture ratio with each repetition of said preparing and measuring steps;

- generating a trend profile model based on the controlled variations in mixture ratio;

- calculating a plurality of model p-values, each model p-value generated based

on a comparison between a characteristic response signature, generated from characteristic values of one of the selected characteristics across all samples, with the trend profile model;

    sorting the calculated model p-values; and

    plotting the sorted model p-values against the ranks of the sorted p-values, based on the order of the sorted p-values.

27. A system for validating or calibrating a plotted curve of sorted p-values against the ranks of the p-values based on the order of the sorted p-values, wherein the p-values are calculated with regard to characteristic signature profiles each generated from a plurality of property values from a plurality of samples, and wherein each said p-value, as statistically calculated, represents the probability that the corresponding characteristic signature profile does not match a predefined signature profile, the system comprising:

    means for selecting a plurality of characteristics from a set of characteristic properties from the samples;

    means for preparing a sample as a mixture having two types of tissue mixed at a controlled mixture ratio;

    means for measuring the selected characteristics in the prepared mixture;

    means for repeating said preparing and measuring steps, while varying the controlled mixture ratio with each repetition of said preparing and measuring steps;

    means for generating a trend profile model based on the controlled variations in mixture ratio;

    means for calculating a plurality of model p-values, each model p-value generated based on a comparison between a characteristic response signature, generated from characteristic values of one of the selected characteristics across all samples, with the trend profile model;

    means for sorting the calculated model p-values; and

    means for plotting the sorted model p-values against the ranks of the sorted p-values, based on the order of the sorted p-values.

28. A method for distinguishing differentially-expressed genes based on plotting one set of expression level values against another set of corresponding expression level values, the method comprising the steps of:

measuring an expression level for each of one or more genes for first and second samples, respectively;

plotting the measured expression levels for the first sample against the measured expression levels for the second sample;

repeating said measuring and plotting steps to establish a number of replicates of the measured expression levels;

determining whether a particular gene from a first sample is differentially expressed relative to the same gene from the second sample, based upon the values of the measured expression levels and their replicates for the particular gene.

29. The method of claim 28, wherein said determining is based on a noise cloud generated by plotting the measured expression level and its replicates with regard to the particular gene in the first sample, against the measured expression level and its replicates with regard to the particular gene in the second sample, wherein the particular gene is determined to be differentially expressed when said less than a predefined percentage of said noise cloud intersects a line representing neutral genes.

30. The method of claim 29, wherein said predefined percentage is five percent at a p-value of 0.05.

31. The method of claim 28, wherein said determining is based on scaling the measured expression level of the particular gene in each of the first and second samples by noise factors characterized by the respective replicates to produce standardized expression levels for the particular gene with regard to the first and second samples, wherein the particular gene is determined to be differentially expressed when said standardized expression levels are plotted as a distance from a



line representing neutral genes that represents a p-value of about .05 or less.

32. The method of claim 28, carried out in multi-dimensional space with regard to greater than two samples.

33. A computer readable medium carrying one or more sequences of instructions for distinguishing differentially-expressed genes based on a distinguishing differentially-expressed genes based on plotting replicates of expression level values against corresponding replicates of another set of expression level values, wherein execution of one or more sequences of instructions by one or more processors causes the one or more processors to perform the steps of:

- plotting an expression level of each of one or more genes for a first sample against an expression level for each of the same one or more genes in a second sample;

- plotting one or more replicates of said expression levels; and

- determining whether a particular gene from a first sample is differentially expressed relative to the same gene from the second sample, based upon the values of the measured expression levels and their replicates for the particular gene.

33. A system for distinguishing differentially-expressed genes based on plotting one set of expression level values against another set of corresponding expression level values, the system comprising:

- means for plotting an expression level of each of one or more genes for a first sample against an expression level for each of the same one or more genes in a second sample;

- means for plotting one or more replicates of said expression levels; and

- means for determining whether a particular gene from a first sample is differentially expressed relative to the same gene from the second sample, based upon the values of the measured expression levels and their replicates for the particular gene.